rated aqueous NaCl and the temperature of the apparatus raised to about ambient temperature (20° to 25°).

After four to six hours at ambient temperature, the dialysate is exchanged for 0.5 percent formaldehyde in a phosphate buffer of about pH 8.0. The dialysis is continued for four hours, at which time the dialysate is replaced by a fresh formaldehyde solution. The dialysis bag now contains moderately constituted dense fibrous micropolymers and some flocculent white material which collects at the bottom of the dialysis bag. The bag is stirred an additional four hours at low speed (approximately 30 rpm) while maintained in the dialysis solution. It is then removed and the small amount of flocculent material separated, followed by reimmersion of the micropolymer fraction in the bag in 1 mM aqueous acetic acid. The solution is cooled to 4° and spun at low speed for an additional four to six hours. After removal of the dialysis bag from the solution, the fibrous micropolymers are collected by centrifugation. They may then be used directly, or stored wet at 4°, or alternatively freeze-dried for indefinite storage.

To prepare a film, the aqueous acetic acid solution containing the fibrous micropolymers may be mixed with collagen in solution to provide a mixture at a desired concentration, usually from about 0.2 to 2% by weight. The solution may be extensively homogenized, preferably in vacuo, employing a degassed suspending medium i.e. aqueous acetic acid. The solution is preferably cooled to 4° and then pumped onto plates in a laminar flow hood at 33° and dried. Further cross-linking can be achieved by exposing the layer to formaldehyde fumes. Successive layers may then be poured over the original layer, with various buffers added to the suspending solution for generating layers of gel-like consistency. The dry sheets are exposed to concentrated ammonia vapor to achieve neutralization, followed by an aqueous acetone (1:1) rinse. The resulting membranes can be sterilized by gas, or exposure to irradiation, heat at 120° C. in vacuo using e.g. gamma-radiation or ultraviolet light. The sterilized membranes are then lyophilized and packaged so as to maintain their asceptic condition.

A burn dressing was prepared as follows. NFMs were dispersed in water, spun down and the process repeated. The collagen was then dispersed in water at a concentration of 20 mg/ml by homogenization. The dispersion was freed of dissolved gases by applying a mild vacuum, followed by pouring the solution into 100×200 mm pans to provide about 1 g of solids in the tray. The dispersion is then concentrated by slowly evaporating the water in a laminar flow hood under ambient condition. The dispersion is then lyophilized to form a foam, followed by cross-linking the foam by treating it with a 0.1 weight percent formaldehyde solution of 1:1 v/v acetone:water for 20 minutes. The foam is then washed with water.

A collagen film is then laminated to the foam as follows. The film precursor is prepared by dispersing a 1:4 weight ratio of noncross-linked NFM with cross-linked NFM. The cross-linked NFM is obtained by treating NFM with a 0.1 weight percent formaldehyde aqueous solution, 0.2 M in disodium phosphate for 20 minutes. Dispersion was achieved by homogenization to provide a concentration of 10 mg/ml.

After removing dissolved gases by applying a light vacuum, the dispersion is introduced into a tray to provide a layer of about 400 mg solids/200 cm^2. The slurry is then frozen at −20° C. The water-washed foam prepared above is applied directly to the solid slurry, entrapped air squeezed out, and then the water is removed by maintaining the laminate at 33° C. until dry. After rehydration with water for one hour, the laminate is lyophilized and then sterilized.

The subject invention provides for nonantigenic atelopeptide collagen in the form of fibrils and fibers which may be used for fabrication of a wide variety of articles or may be used directly as gels for coating various wounds or injuries, e.g. burns, for replacement of vitreous, or the like, for preparation of packings or implants or for the production of membranes, bags, films, sutures, strands, dressings, prosthetic devices or the like for replacement of defective or absent connective tissue e.g. skin, bone, tendon or other mammalian structural members.

The atelopeptide collagen of this invention can also be used for cosmetic purposes, particularly by plastic surgeons for enhancing or forming breasts, in jaws or in other mammalian structural members to modify the size, shape, contour or the like. In accordance with this invention, a collagenous material is achieved which is not rejected when implanted in human or other animals and, depending upon the manner of cross-linking, can have a wide variety of tensile properties approaching or exceeding those of naturally occurring collagen. The manner in which the collagenous fibril is prepared allows for a great degree of flexibility in its subsequent employment, either by itself or in combination with collagen in solution.

The procedures employed in accordance with this invention remove almost all or all of the noncollagen protein and materials other than protein, as well as the immunogenic telopeptides. The resulting atelopeptide collagen is substantially freed of the immunogenic procedures and mechanical and chemical treatment, the atelopeptide collagen is oriented, so as to form fibers which resemble natural collagen fibers. These fibers may then be cross-linked in accordance with known techniques to provide filaments and fibers of varying physical characteristics, as required, resembling or being superior to natural collagen.

The atelopeptide collagen of this invention upon implantation or application to living tissue supports invasion by the host cells. Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be obvious that certain minor changes and modifications may be introduced within the scope of the appended claims.

We claim:

1. A method of preparing fibers of atelopeptide collagen having physical properties resembling natural collagen fibers which comprises:

inducing slow desolubilization of atelopeptide collagen from an aqueous solution of atelopeptide collagen while subjecting said solution to a directionally uniform mild shear force of about 30 to about 5000 dynes/cm^2 whereby fibers of atelopeptide collagen are formed.

2. A method according to claim **1**, wherein said inducing is achieved by having an initial acidic medium to which is slowly added an inorganic alkaline salt.

3. A method according to claim **2**, wherein said inorganic alkaline salt is a phosphate.

4. A method according to claim **1**, wherein said aqueous solution is contained in a dialysis bag which is